Prevalence of Sarcopenia and Predictors of Skeletal Muscle Mass in Healthy, Older Men and Women

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Background. Sarcopenia refers to the loss of skeletal muscle mass with age. The objective of this study was to determine the prevalence of sarcopenia in a population of older, community-dwelling research volunteers.

Methods. Appendicular skeletal muscle mass was measured by dual x-ray absorptiometry in 195 women aged 64 to 93 years and 142 men aged 64 to 92 years. We defined sarcopenia as appendicular skeletal muscle mass/height^2 (square meters) less than 2 standard deviations below the mean for young, healthy reference populations. We used two different reference populations and compared prevalence in our population to that reported in previous studies. Body mass index (BMI) was calculated and physical activity and performance were measured with the Physical Activity Scale for the Elderly, the Short Physical Performance Battery, and the Physical Performance Test. We measured health-related quality of life by using the SF-36 general health survey. Serum estrone, estradiol, sex hormone-binding globulin, parathyroid hormone, and 25-hydroxy vitamin D were measured in all participants and bioavailable testosterone was measured only in men. Leg press strength and leg press power were determined in men.

Results. The prevalence of sarcopenia in our cohort was 22.6% in women and 26.8% in men. A subgroup analysis of women and men 80 years or older revealed prevalence rates of 31.0% and 52.9%, respectively. In women, skeletal muscle mass correlated significantly with BMI and levels of serum estrone, estradiol, and 25-hydroxy vitamin D; in men, it correlated significantly with BMI, single leg stance time, leg press strength, leg press power, SF-36 general health score, Physical Performance Test total score, and bioavailable testosterone levels. With the use of linear regression analysis, BMI was the only predictor of appendicular skeletal muscle mass in women, accounting for 47.9% of the variance ($p < .05$). In men, BMI accounted for 50.1%, mean strength accounted for 10.3%, mean power accounted for 4.1%, and bioavailable testosterone accounted for 2.6% of the variance in appendicular skeletal muscle mass ($p < .05$).

Conclusions. Sarcopenia is common in adults over the age of 65 years and increases with age. BMI is a strong predictor of skeletal muscle mass in women and men. Strength, power, and bioavailable testosterone are further contributors in men. These data suggest that interventions to target nutrition, strength training, and testosterone replacement therapy should be further investigated for their role in preventing muscle loss with age.

S ARCOPENIA is a word coined from Greek by Irwin H. Rosenberg in 1988 (1); *sarx* means flesh and *penia* means loss (2). Sarcopenia refers to the age-related decline in lean body mass that affects the functional capacity of older adults (1). The age- and sex-adjusted prevalence of sarcopenia varies from 6% to 24%, depending on the definition and measure of muscle mass used (3–5). Further, in an older cohort in New Mexico (4), the prevalence of sarcopenia increased to >50% after the age of 80 years. Coincident with this decline in muscle mass is a decline in function. The Framingham Disability Study found that the ability to perform heavy household work, walk one half mile, and climb stairs declined with age and that participants aged 75–84 were more likely to require help with activities of daily living (6). In addition, leg extensor power has been associated with better performance in chair rising, stair climbing, and walking in older community-dwelling adults (7). Finally, sarcopenia has been associated with disability in both men and women (4,8). A greater understanding of age-related loss of lean body mass could have a dramatic impact on older adults if sarcopenia research leads to maintenance or improvement in functional ability.

Age-related decline in lean body mass was recognized long before the term *sarcopenia* was coined. In 1970, Forbes and Reina concluded that both age and sex should be considered in determining drug dosages and nutritional requirements based on the decline in lean body mass (9). Bortz, in 1982, commented that disuse of muscle resulted in loss of lean body mass (10). Rosenberg sought to rekindle research interest in this field by creating the term *sarcopenia* (1) and, in 1996, he noted that sarcopenia research had increased since the application of the term (2). Rosenberg also raised the question of whether sarcopenia is a "normal" part of aging or a disease state. He compared muscle wasting with bone loss and suggested that if decline in muscle mass could predict disability or mortality, then it would be important to identify this decline before functional loss was severe (2). To prevent or treat sarcopenia, there must be identification of predictors of skeletal muscle mass. Gallagher and colleagues found that gender greatly influenced muscle mass and that, with age, men experience a decline in muscle mass almost twice that of women (11). Free testosterone, physical activity, cardiovascular disease, and insulin-like growth factor-1 (IGF-1) are significant predictors of muscle mass in men, and total fat mass and physical activity were significantly associated with muscle mass in women (12).

Our objective in this study was to confirm sarcopenia prevalence rates reported by Baumgartner and colleagues

(12), who established prevalence rates in a large cohort on the basis of calculations of skeletal muscle mass from a subsample of 199 men and women. We determined the prevalence of sarcopenia in a large cohort of healthy, community-based older adults who had all undergone body muscle mass measurement, and we assessed the predictors of sarcopenia in this population.

METHODS

We completed a cross-sectional analysis of data from four longitudinal studies conducted at the Claude Pepper Older Americans Independence Center and The Center on Aging at the University of Connecticut Health Center (13–15). For this study, we included men and women and used only baseline data that were collected by trained personnel following standardized protocols.

All volunteers were relatively healthy; they could have no disease that would affect bone metabolism and could not be taking prescribed medication known to affect bone metabolism. Only Caucasian participants were included in analysis because of the small number of non-Caucasian volunteers. Baseline data collection included determination of body composition measured by dual x-ray absorptiometry, as well as determination of height, weight, dietary calcium, and dietary protein.

Body Composition

Total and regional lean tissue masses of volunteers were determined from whole body dual x-ray absorptiometry, using a DPX-IQ scanner (GE Medical Systems Lunar, Madison, WI); all scans were obtained by the same certified technician. Whole body scans provided total lean body mass (in kilograms), total fat mass (in kilograms), and total body bone mineral content (also in kilograms). Appendicular skeletal muscle mass (ASM) was determined by combining the lean tissue mass of the regions of the arms and legs, excluding all other regions from analysis (16). ASM represents 75% of the total skeletal muscle mass (TSM); therefore, we estimated TSM (16) by using the equation TSM $=$ ASM $\times$ 1.33. We adjusted ASM and TSM for height by dividing each by height squared (square meters), that is, ASM/Ht^2 and TSM/Ht^2 (3,4). We defined sarcopenia as skeletal muscle mass > 2 standard deviations below the sex-specific young-normal mean for estimates of skeletal muscle mass (4). Normative levels for ASM/Ht^2 and TSM/Ht^2 for our analysis are taken from previous studies (3–5).

Physical Activity, Performance Measures, and Quality of Life

We estimated physical activity by using the Physical Activity Scale for the Elderly (17). Leg extension strength and power were measured on the Keiser sitting leg press; 1 repetition maximum (18) intratester and intertester variability was $<10\%$. The Short Physical Performance Battery and single leg stance time were used to assess lower extremity function (19). The Physical Performance Test (7 item), a direct observation of activities of daily living, was also used to assess function (20). The SF-36 health survey measured health-related quality of life (21).

Biochemical Measurements

Blood and urine samples were collected between 7 AM and 9 AM after subjects underwent a 10- to 12-hour fast. Urine and serum were divided into 0.5-ml aliquots and stored at $-70°C$. 25-hydroxy vitamin D (25OHD) was measured by competitive protein bind with an intra-assay coefficient of variation of $<10\%$ (Endocrine Sciences Inc., Calabasas Hills, CA). Serum estrone and estradiol (E_1 and E_2, respectively) were performed in the General Clinical Research Center core lab by using radioimmunoassay (Diagnostic Systems Lab, Inc., Webster, TX), with an intra-assay variability of $<10\%$. The detection limit of the E_2 assay is 2 pg/ml. In men, total and bioavailable testosterone and sex hormone-binding globulin (SHBG) measurements were performed at Endocrine Sciences. Testosterone levels were measured by radioimmunoassay, SHBG by competitive binding assay, and bioavailable testosterone by competitive binding of the non-SHBG-bound portion of testosterone following ammonium sulfate percipitation of the SHBG-bound steroid (22). Intra-assay variability of the testosterone assay is $<7\%$, bioavailable testosterone is $<4\%$, and SHBG is $<10\%$. Samples for off-site assay were shipped on dry ice by overnight mail. For women, SHBG was measured by immunoradiometric assay (Diagnostic Products Co., Los Angeles, CA) in the General Clinical Research Center core lab with an intra-assay variability of $<4\%$.

Statistical Analysis

We used Pearson correlation coefficients to determine the association between ASM/Ht^2 and sex hormone levels, 25OHD, parathyroid hormone, Physical Activity Scale for the Elderly, physical performance measures, power, strength, and health perception. We used multiple linear regression to evaluate the contribution of sex hormones, 25OHD, parathyroid hormone, strength, power, physical activity and performance, or health insight to variance in ASM/Ht^2. The SPSS statistical software package was used for all analyses (SPSS, Inc., Chicago, IL).

RESULTS

Three hundred thirty-seven individuals were included in the study: 195 women and 142 men. Characteristics of older adult volunteers included in the study are presented in Table 1. The prevalence of sarcopenia in our group and the Baumgartner cohort are presented in Table 2, using the definition of sarcopenia proposed by Baumgartner and colleagues (4). With the selection of the subgroup over 80 years, the prevalence of sarcopenia increased to 31.0% in women ($n = 29$) and 52.9% in men ($n = 19$).

Different factors correlated with ASM/Ht^2 in men and women (Table 3). Body mass index (BMI) correlates highly with ASM/Ht^2 in both sexes. In women, E_1 and E_2 also correlated with ASM/Ht^2. There was a significant inverse relationship between ASM/Ht^2 and 25OHD in women. In men, ASM/Ht^2 correlated with single leg stance time, leg strength, leg power, general health, Physical Performance Test total score, and bioavailable testosterone.

In women, multiple linear regression analysis with ASM/Ht^2 as the dependent variable revealed a positive association with BMI only. This model accounted for 47.9% of the vari-

Table 1. Descriptive Characteristics of a Healthy Caucasian Cohort Aged ≥ 65 y

Characteristic	Women	Men
Age (y)	75.0 (4.7)	73.8 (5.3)
BMI (kg/m^2)	26.5 (5.1)	26.5 (3.9)
ASM (kg)	15.2 (1.9)	23.9 (3.4)
ASM/Ht^2 (kg/m^2)	6.0 (0.7)	7.8 (0.9)
Activity/Phys. performance		
PASE total score	123 (58)	168.1 (56.4)
SPPB total score	10.5 (1.4)	11.1 (1.3)
Rise time out of chair (s)	12.9 (3.5)	11.2 (3.8)
8-ft walk time (s)	2.6 (0.7)	2.4 (0.4)
PPT total score	23.6 (2.7)	23.8 (2.0)
Health perception		
PCS	49.3 (7.7)	46.5 (9.5)
MCS	56.5 (6.0)	57.3 (5.8)
Biochemical markers		
Estrone (pg/ml)	23.7 (12.0)	30.0 (18.7)
Estradiol (pg/ml)	8.5 (4.1)	19.3 (13.5)
SHBG (nmol/l)	185.9 (147.7)	50.8 (21.1)
PTH (pg/ml)	41.6 (30.5)	40.9 (21.4)
25OHD (ng/ml)	23.1 (8.1)	27.0 (8.2)
Testosterone (ng/dl)	ND	436 (176)
Bioavailable testosterone (ng/dl)	ND	106 (40)
Physiologic markers		
Leg Press strength (N)	ND	879 (310)
Leg Press power (W)	ND	320 (138)

Notes: Results are reported as mean (standard deviation). ASM = appendicular skeletal mass; BMI = body mass index; PASE = Physical Activity Scale for the Elderly; SPPB = Short Physical Performance Battery; PPT = Physical Performance Test; PCS = physical component score; MCS = mental component score; SHBG = sex hormone-binding globulin; PTH = parathyroid hormone; 25OHD = 25-hydroxy vitamin D; and ND = not done.

Table 3. Correlations Between ASM Corrected for Height and Measured Parameters In Women and Men Aged ≥ 65 y

Group	ASM/Ht^2
Women	
BMI	0.695**
PASE total score	0.023
Rise time out of chair	0.055
GHS, SF-36	−0.020
Estrone	0.244*
Estradiol	0.357**
25OHD	−0.161*
Men	
BMI	0.682**
Single leg stance time	0.207*
Leg press strength	0.504**
Leg press power	0.409**
GHS, SF-36	0.176*
PCS, SF-36	0.123
MCS, SF-36	0.082
PPT total score	0.221*
Estrone	0.034
Estradiol	0.047
Biotestosterone	0.357**
25OHD	−0.075

Notes: ASM = appendicular skeletal muscle mass; BMI = body mass index; PASE = Physical Activity Scale for the Elderly; GHS = general health score; SF-36 = Medical Outcome Survey Short Form 36; PCS = physical component score; MCS = mental component score; PPT = Physical Performance Test; and 25OHD = 25-hydroxy vitamin D.

*$p < .05$; **$p < .001$.

ance in ASM/Ht^2 in women ($B = 3.52$, $p < .001$). In men, a positive association was found between ASM/Ht^2 and BMI, strength, power, and bioavailable testosterone ($B = 3.06$, $p < .001$). This model explained 67.1% of the variance in ASM/Ht^2. When each variable was examined independently, BMI accounted for 50.1%, mean strength accounted for 10.3%, mean power accounted for 4.1%, and bioavailable testosterone accounted for 2.6% of the variance in ASM/Ht^2 (all $p < .005$).

DISCUSSION

We confirmed the prevalence of sarcopenia reported by Baumgartner, using body mass measurement from the entire cohort. The prevalence rates in our cohort were over 20% and confirm that skeletal muscle mass is common in older

Table 2. Sarcopenia Prevalence in our Cohort Versus the Baumgartner Cohort

Group	Our Cohort (%)	Baumgartner Cohort (%)
Women	22.6 ($n = 195$)	33.9 ($n = 173$)
Men	26.8 ($n = 142$)	28.5 ($n = 205$)

Notes: Sarcopenia prevalence was measured in healthy Caucasian research volunteers, using the definition proposed by Baumgartner and colleagues (5): appendicular skeletal muscle mass/height^2 (kg/m^2) < 2 standard deviations below the mean value for young adults. Both cohorts were aged ≥ 65.

individuals. The prevalence of sarcopenia differs, depending on which normative data are used: those of Baumgartner and colleagues (4), Tanko and colleagues (5), or Melton and colleagues (3). Tanko's group used the definition of sarcopenia used by Baumgartner and colleagues (4), but with a different reference population to establish normative data; this population included only women. Using the cutoff value of 5.4 kg/m^2 established by Tanko, we found that the prevalence of sarcopenia in our female cohort was 22.7%. In contrast, using the definition of sarcopenia defined by Melton's group and using TSM/Ht^2 and normative data from their cohort, we found that the prevalence of sarcopenia in our study was 1.5% for women and 11.3% for men.

The prevalence of sarcopenia in our cohort varies from that reported by others. The differences may be explained by different definitions of sarcopenia, differences in populations being studied, or reference populations. Baumgartner and coworkers defined sarcopenia as ASM/Ht^2 < 2 standard deviations below the mean of young healthy adults, a definition analogous to that of osteoporosis using bone mineral density (4). The prevalence of sarcopenia in our cohort is less than that found by Baumgartner's group, who studied a population-based sample. We, in contrast, evaluated research volunteers with the potential for greater health caused by selection bias. The differences may be explained by the differences in subject selection. Baumgartner and colleagues also measured muscle mass in a subgroup and estimated skeletal muscle mass for the entire cohort, potentially introducing error (4).

As already mentioned, Tanko and colleagues used the

same definition as Baumgartner, but a different reference population (5). They found the prevalence of sarcopenia to be 12.3%; their population seems the most similar to the population we studied, although differences do exist. Differences in prevalence rate between our groups may be explained by the smaller sample size in the study by Tanko and a more strict inclusion criteria relative to our parameters, most notable being the requirement of "no history of reduced ambulation or prolonged immobilization" (5); our inclusion criteria allowed subjects who were able to ambulate with assistive devices. Further, we did not exclude for prior history of decreased ambulation or prolonged immobilization.

Melton and colleagues (3) defined sarcopenia by using total rather than skeletal muscle mass (TSM = ASM × 1.33). Using this definition for sarcopenia, we found that prevalence rates in our cohort were 1.5% for women and 11.3% for men (as already mentioned) compared with their findings of 11.8% for women and 16.0% for men. Others have suggested that estimation of total body skeletal muscle mass with this formula may introduce error as a result of potential increases in water or fat content in aging muscle (23,24). In addition, the reference population from the Mayo group included subjects up to 50 years of age. Two other studies (5,25) have found that age-associated decline in skeletal muscle mass begins in the fifth decade; therefore, inclusion of older subjects in the reference population could lower reference population norms, leading to lower estimation of prevalence in the elderly cohort. Finally, Melton and colleagues included both community-dwelling and institutionalized individuals, whereas our cohort included only community-dwelling research volunteers (3).

Our study and the work of others reveal that a substantial portion of older individuals have sarcopenia, even in studies evaluating healthy, older groups. These findings now require longitudinal data for us to understand what impact low muscle mass has on health-related outcomes such as quality of life, disability, and mortality. Baumgartner and colleagues have begun this work by establishing higher disability rates in those with lower skeletal muscle mass (4). Similarly, Freid and coworkers have found higher disability and mortality rates in frail older adults, and their definition of frailty incorporates features that are associated with lower skeletal muscle mass, including grip strength, walking speed, weight loss, and sense of exhaustion (26).

BMI was the only predictor of skeletal muscle mass for women in our study and explained 47.9% of the variance. These findings are consistent with the findings of others. Baumgartner and colleagues found percent fat and knee height to be predictors of skeletal muscle mass in women accounting for 48% of the variance (12). Similarly, Tanko and coworkers found that age, height, and weight explained 58% of the variance (5). Further, these results are consistent with those of Janssen and colleagues (25), who found that ∼50% of the variance in skeletal muscle mass was accounted for by height and weight. These results suggest that exploration of nutritional factors such as protein intake or the inflammatory process associated with cachexia may assist in understanding the components of sarcopenia. Large decreases in protein intake result in decreased strength,

skeletal muscle fibers, skeletal muscle mass, and IGF-1 levels in postmenopausal women (27–29). In addition, deficiency in vitamin D is associated with poor strength and balance (30,31), although the relationship of vitamin D stores to muscle size or mass is unknown. In longitudinal studies, catabolic cytokines are associated with loss in lean body mass and increased resting energy expenditure in patients with rheumatoid arthritis and HIV infection (32,33), and the catabolic cytokines have also been associated with lower ASM in a cross-sectional analysis of healthy older individuals (34).

In our cohort of men, BMI accounted for 50.1% of the variance in skeletal muscle mass, similar to the findings of Baumgartner and colleagues (4) and Janssen and colleagues (25). In addition, mean strength accounted for 10.3% and power accounted for 4.1% of the variance in our group of men. Our results are also consistent with those of others who found a strong correlation between muscle mass and muscle strength in older men (35,36). Baumgartner and coworkers found that muscle mass was an important predictor of grip strength in men (12). Muscle mass has been related to function; Skelton and colleagues reported that isometric knee extensor strength was associated with a decrease in chair rise time and that power was associated with a decrease in chair rise time and increase in step height (37). Other studies demonstrated that strength and power were associated with walking speed and other functional outcomes (7,38,39). In addition, Baumgartner and colleagues also found physical activity to be a predictor of skeletal muscle mass in women, an association we did not find (12), possibly a result of the healthier volunteers we studied and the use of different physical assessment instruments (17). Finally, studies of strength training in older men and women have demonstrated significant gains in strength and lean tissue mass (18,40), suggesting that strength training may be useful in preventing functional decline.

Bioavailable testosterone also predicted skeletal muscle mass in our male cohort, explaining a small portion of the variance. Testosterone has known anabolic properties in muscle. Bioavailable testosterone is related to lower extremity strength and function (41,42), and testosterone treatment in older hypogonadal men increased hand-grip strength (43,44) and lower extremity muscle strength (13,45). Thus, testosterone may be one part of a multifactorial system affecting skeletal muscle mass and, consequently, influencing strength and function in older men. We did not collect data on testosterone levels in women, but in previous studies total lean mass correlated with bioavailable testosterone in postmenopausal women (46), and lower body strength increased in women treated with estrogen and androgen preparation (47). Further study is needed to determine the role of androgens in preserving muscle mass and, consequently, function in postmenopausal women.

Conclusion

Our study demonstrated that the prevalence of sarcopenia is more than 20% in healthy, independent older adults and that sarcopenia increases with age. The impact of preventing sarcopenia on long-term function and disability is not known, but our work suggests that nutrition, exercise, and

potentially hormone replacement therapy may be important factors to consider.

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